

Remarks/Arguments

Claims 1 to 11, and 13 to 23 are pending. Claim 1 has been rejected, and Claims 2 to 11 and 13 to 23 have been objected to in the Office Action dated November 14, 2008. A minor amendment has been made to Claim 1, and enter of the amendment is requested.

Claim 1 has been rejected under 35 U.S.C. § 103(a) as being unpatentable over *Ding et al.* (see CAPLUS). Applicant traverses this rejection.

Ding et al. is not a valid or viable reference against applicant's Claim 1; therefore this obviousness rejection fails and should be withdrawn.

Ding et al. (the copy supplied by the Examiner) contains the statement:

"COPYRIGHT 2008".

The heading of the cover page of the Office Action states that the filing date of this U.S. application is:

"02/28/2006".

Since *Ding et al.* has a copyright notice date of 2008, *Ding et al.* has a publication date of 2008. There is nothing on *Ding et al.* to prove that it has an earlier publication date.

Therefore, *Ding et al.* has a publication date after even applicant's U.S. filing date.

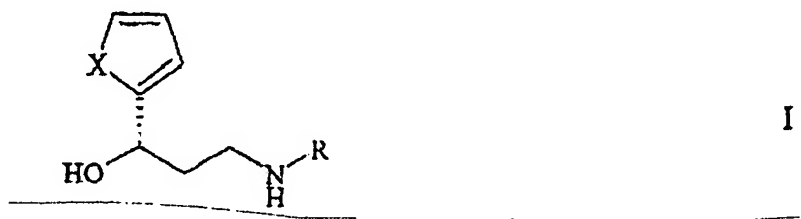
Accordingly, *Ding et al.* is not a reference under Section 102 or Section 103(a) against Claim 1 (or any other of applicant's claims). This also means that the objection against the other claims also fails. Applicant requests that this case be allowed and passed to issue.

The burden of proof is on the Examiner to prove, if such can be done, that Ding et al. has an earlier publication date than the 2008 copyright notice on it. Ding et al. is worthless as a reference unless the Examiner can prove that Ding et al. has a publication date before September 1, 2003. (Applicant might be able to show invention even before that date.)

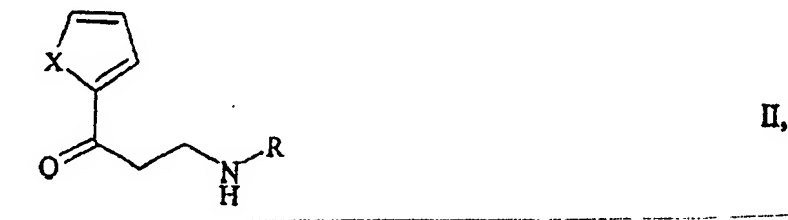
Ding et al. is an abstract of Chinese Patent No. 1356334 A. Ding et al. is not Chinese Patent No. 1356334 A (for example, Ding et al. does not even contain a claim). It is clear from viewing Ding et al. that Ding et al. (an abstract) does not contain all of the information contained in Chinese Patent No. 1356334 A. This obviousness rejection is not based on Chinese Patent No. 1356334 A. If the Examiner ever bases an obviousness rejection on Chinese Patent No. 1356334 A, applicant will insist that the involved Office Action not be final.

If the Examiner proves that Ding et al. had a publication date that made it a prior art reference to applicant's Claim 1, note that the Examiner has not carried his burden of proof to factually show in the record that Claim 1 is obvious, prima facie or otherwise, to one ordinarily skilled in the art based on Ding et al.

The Office Action stated: that applicant claims a process for the preparation of a chiral compound of formula:



wherein X represents S or O and R represents hydrogen, C₁₋₆ alkyl, C₃₋₅ cycloalkyl, aryl or aralkyl, each aryl or aralkyl being optionally further substituted as defined in claim 1, which process comprises the asymmetric hydrogenation of a compound of formula II:



wherein X and R are as defined above in the presence of a transition metal complex of a chiral bidentate phosphine ligand, that is a stabilizing, and optionally a base.

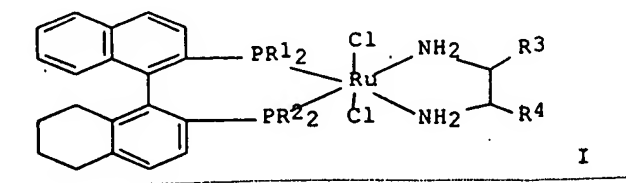
Applicant does not disagree with this general summary of the subject invention.

To show justification of the rejection of Claim 1 under Section 103(a), the Examiner immediately went into an attempt (which fails on its face) in the Office Action to show establishment of a prima facie showing obviousness of Claim 1. This effort failed – the Examiner has not factually established in the record a showing of prima facie obviousness, let alone sufficient or any support of obviousness to one ordinarily skilled in the art. The Examiner has not carried his burden of proof under Section 103(a).

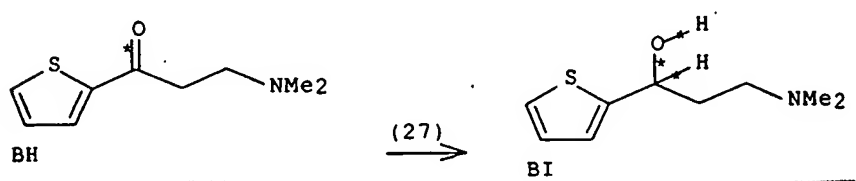
Section 103(a) requires that the Examiner factually resolve in the record the level of ordinary skill in the art – this has not been done in the record, so this Section 103(a) rejection fails from the start. There can be no valid showing of obviousness and/or prima facie obviousness unless, and until, the Examiner has factually resolved in the record the level of ordinary skill in the art. The Examiner has not done this as required

by the Supreme Court Graham and KSR decisions and Patent Office policy. The Patent Office also requires that the Examiner's analysis and supporting facts that the Examiner uses be made of record.

The Office Action stated, regarding the scope and content of the prior art, that *Ding et al.* teaches an asymmetric catalytic hydrogenation of ketones by using a Ru complex of formula:



as a catalyst; and that the various reactions disclosed in the reference include:



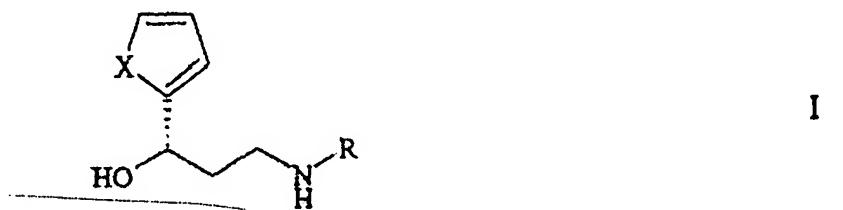
. Applicant

does not disagree with the Examiner's very general summary of a selected portion of that which is disclosed in *Ding et al.* However, applicant points out that *Ding et al.* is not prior art to applicant's claimed invention. Also, catalytic activity is unpredictable so the catalytic process of *Ding et al.* is of little or no value in the attempt to render applicant's claimed process to one ordinarily skilled in the art.

Regarding the difference between the prior art and the claims, the Office Action stated: that the difference between the prior art of *Ding et al.* and the instant invention is that the amine in the structure in the instant compounds is a methyl amine (secondary) whereas the amine in the prior art is a diethyl amine (tertiary). Applicant concurs that

this is a significant difference, one of many, between the subject invention and *Ding et al.*

Regarding prima facie obviousness and the rational motivation, the Office Action stated: that applicant is claiming a process for preparing a compound of formula:



wherein the variables are as defined in claim 1 which the process comprises the asymmetric hydrogenation of a compound of formula II in the presence of a transition metal complex of a chiral bidentate phosphine ligand; that the prior art reference of *Ding et al.* teaches a similar process wherein the amine group in the compound is a dimethyl amine (tertiary) versus a methyl amine (secondary) in the instant compound. Applicant agrees that one of the differences between the similar processes disclosed in the subject invention and *Ding et al.* is that the amine group in the compound is a dimethyl amine (tertiary) in *Ding et al.* versus a methyl amine (secondary) in the compound disclosed in the subject invention.

Applicant points out that *Ding et al.* has to protect a hydrogen on the amine group with a protective group, for example, a methyl group. In contrast, applicant's claimed invention does not have to have a protective group for the hydrogen on the amine group. Thus, applicant's claimed process invention has such unexpected advantage over *Ding et al.* *Ding et al.* does not suggest advantage, and even directs one ordinarily skill in the art away from applicant's claimed invention. The Examiner has not factually

established in the record either a case of obviousness or a showing of prima facie obviousness.

Ding et al. has to remove the protective group as one of the final steps before the final active compound is obtained. Applicant's claimed process does not use a protective group on the hydrogen on the amine. Therefore, applicant's claimed process is not obvious to one ordinarily skilled in the art.

The Office Action stated that in Ex parte Bluestone, 135 USPQ 199, it was well established that the interchange of alkyl and hydrogen is obvious in and of itself and in addition secondary and tertiary amines are interchangeable. Applicant traverses this statement as being clearly in error. Applicant has shown that the premise of the Bluestone case and the Examiner is clearly incorrect when it comes to matters as free hydrogen and the use of protective group in its place.

The basic premise of the Bluestone case is not viable scientifically and technically, and may only be viable for the specific facts of such case. Start with -OH ; if the substituent is -H , the result is water, which man needs and is harmless to man; however, if the substituent is -CH_3 , the result is CH_3OH , which is poisonous and deadly to man; and, if the substituent is $\text{-C}_2\text{H}_5$, the result is $\text{C}_2\text{H}_5\text{OH}$, which man drinks and forms one of basis of much of his social activity.

The Supreme Court Graham decision is dated 1966, which is later than the Bluestone case. The Supreme Court's requirement in the Graham decision was that its three prongs of factual inquiry had to first be determined to form the base for any obviousness determination, and only then could secondary considerations like that in the

Bluestone case, if scientifically sound, could be considered. The Supreme Court trumps a lower court decision, particularly one earlier in time.

The Office Action stated: that, for example, it is obvious to prepare a beta amino ketone wherein the amine group is substituted with an alkyl group (i.e., methyl) using asymmetric hydrogenation in the presence of a transition metal complex of a chiral bidentate phosphine ligand when the art teaches a similar process wherein the amine group in the ketone is disubstituted with dimethyl with a reasonable expectation of success; that, specifically, a monomethyl substituted beta-amino ketone and a dimethyl substituted beta-amino ketone are considered homologues and are obvious absent unexpected results; that, therefore, it would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to prepare adjacent homologues by using asymmetric hydrogenation based on the teachings of the prior art; and that a strong prima facie obviousness has been established. Applicant traverse this statement as being incorrect in fact and law. For example, methanol is deadly to man and the adjacent homologue ethanol is drunk by man. The Examiner says that something is "obvious" – however, this assertion is meaningless under Section 103(a) since the Examiner has not asserted obviousness to such person (who he has not determined in the record).

The Examiner himself noted that his conclusion regarding monomethyl substituted beta-amino ketone and a dimethyl substituted beta-amino ketone being considered homologues and therefore obvious was contingent upon the absence of unexpected results. But, as is disclosed in the subject specification, the subject invention as claimed in Claim 1 solves a problem in the prior art and is, therefore, an

unexpected result. In lines 24 to 27 on page 4 of the subject specification, it is stated that, “[t]he technical problem to be solved by the present invention was to provide a selective and high-yield process for the asymmetric hydrogenation of N-monosubstituted β -ketoamines to get enantiomerically enriched or enantiomerically pure (S)- or (R)-N-monosubstituted β -amino alcohols without using protective groups for the secondary amino group.” It is further stated in line 31 on page 4 of the specification, that “[t]he problems mentioned above could be solved according to the process of claim 1. “ The secondary amino group is a critical component of the subject invention as it is part of the unexpected result. That is, again, “[t]he technical problem to be solved by the present invention was to provide a selective and high-yield process for the asymmetric hydrogenation of N-monosubstituted β -ketoamines to get enantiomerically enriched or enantiomerically pure (S)- or (R)-N-monosubstituted β -amino alcohols without using protective groups **for the secondary amino group.**” [Emphasis added]

The Examiner has not the above, so the Examiner has not carried his burden of proof.

For the above reasons, applicant disagrees that the subject invention as claimed in Claim 1 is rendered unpatentable as obvious over *Ding et al.*

Applicant requests that this rejection of Claim 1 under 35 U.S.C. § 103(a) be withdrawn.

Dependent Claims 2 to 11 and 13 to 23 have also been objected to as being dependent upon a rejected base claim. Applicant asserts that the instant rejection of Claim 1 presently should be withdrawn for the reasons set out above. Thus, applicant believes that this objection to Claims 2 to 11 and 13 to 23 as being dependent upon a rejected base claim also presently should be withdrawn.

The Office Action stated: that, to overcome this objection, applicant should rewrite said claims in an independent form and include the limitations of the base claim and any intervening claim. Since applicant believes that the rejection of Claim 1 should be withdrawn at present, he does not agree that the dependent claims should be rewritten in independent form to include the limitations of the base claim and any intervening claims.

Thus, applicant requests that this objection to Claims 2 to 11 and 13 to 23 presently be withdrawn.

Applicants thank the Examiner for indicating the allowability of the dependent claims.

Reconsideration, reexamination and allowance of the claims are respectfully requested at present.

Respectfully submitted,

March 16, 2009
Date

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